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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/651,136	08/28/2003	Sandor Sipka	22740-2	8175

24256 7590 10/23/2006

DINSMORE & SHOHL, LLP
1900 CHEMED CENTER
255 EAST FIFTH STREET
CINCINNATI, OH 45202

EXAMINER	
ROONEY, NORA MAUREEN	
ART UNIT	**PAPER NUMBER**
1644	

DATE MAILED: 10/23/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/651,136	SIPKA ET AL.	
	Examiner	Art Unit	
	Nora M. Rooney	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 August 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-21* is/are pending in the application.

4a) Of the above claim(s) *6-9,11,12,14-16,20 and 21* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5,10,13 and 17-19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-21 are pending.

2. Claims 6-9, 11-12, 14-16, 20 and 21 stand withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species, there being no allowable generic or linking claim.

3. Claims 1-5, 10, 13 and 17-19 are under examination as they read on a process for inhibiting allergic disease in a human subject by administering an aerosol spray composition comprising irradiation-detoxified lipopolysaccharide.

4. In view of the amendment filed on 07/27/2006, only the following rejections remain.

5. Applicant's amendment filed 08/02/2006 is acknowledged.

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 1-5, 10, 13 and 17-19 stand rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention for the same reasons set forth in the previous Office Action mailed on 04/24/2006.

Applicant's arguments filed on 08/02/2006 have been fully considered, but are not found persuasive.

Applicant argues that LPS derived from microbial and/or fungal endotoxin are similar in structure and that LPS derived from gram negative bacteria, such as E. coli bacteria, is representative of the entire genus of LPS derived from microbial and/or fungal endotoxins. To support these assertions, applicant has provided the teachings of the Knirel et al. reference, "which disclose the structural similarities of fungal and bacterial LPS" and the teachings of the Trent et al. reference "which discloses that gram-negative bacteria in general have very similar LPS structural properties."

However, it is the Examiner's position that Applicant has no written support in the specification as filed for the genus term LPS derived from microbial and/or fungal endotoxin. The scope of the term reads upon thousands if not millions of LPS molecules isolated from organisms not yet even isolated. In a review of the specification, Applicant has written support only for LPS derived from E. coli bacteria. There is no disclosure of the additional LPS structures from the varied genus Applicant is claiming. Therefore, Applicant is not in a position of the process for inhibiting development of allergic disease using the entire genus of microbial and/or fungal endotoxin.

The Knirel et al. reference does not mention fungus or fungal endotoxin in any way, nor does it provide support for the similarity of fungal endotoxin to bacterial endotoxin. Instead, it provides support on page 3, 4th paragraph, for the definition of LPS as being "the major component of the outer membrane of the **bacterial** cell wall." (Emphasis added.) In the same way, Applicant has not provided support for the claimed genus of LPS from bacterial endotoxin because Applicant has only provided support in the specification for LPS from one type of gram-negative bacteria (E.coli). Additionally, the Examiner is not familiar with the term "fungal endotoxin" or any

"lipopolysaccharide derived from" fungal endotoxin. Please provide a reference showing support for these terms.

Applicant is not in possession of the process for inhibiting development of allergic disease with lipopolysaccharide derived from microbial and/or fungal endotoxin. Instead, the specification and references only provide support for the subgenus of gram-negative bacteria. Accordingly, the claims stand rejected.

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

9. Claims 1-5, 10, 13 and 17-19 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Tulic et al. (reference U on the PTO-892), in view of Matricardi et al. (Reference AO on the IDS submitted 10-4-04), Bertok et al. (Reference AN on the IDS submitted 10-4-04) and Liu et al. (reference V on the PTO-892) for the same reasons set forth in the previous Office Action mailed on 04/24/2006.

Applicant's arguments filed on 08/02/2006 have been fully considered, but are not found persuasive.

Applicant argues that Tulic et al. teaches modification of the inflammatory response in adult mice, unlike the present application, which inhibits allergic disease in neonatal mice. Applicant argues that Bertok et al. discloses the use of detoxified LPS in the pretreatment in various shocks, radiation diseases and infections, but not allergic disease like the present application. Applicant also argues that Liu et al. discloses a review of recent studies on endotoxin exposure, but does not teach the use of irradiation detoxified LPS for decreasing allergy in a neonatal or immature mammal or bird.

Examiner asserts that although Tulic et al. does not specifically treat allergic symptoms of neonates with irradiated LPS, the teachings of Bertok et al, Matricari et al and Liu et al. make it obvious for one of ordinary skill in the art to combine the teachings of the references to arrive at the claimed invention. Bertok et al. teaches on page 223 the use of detoxified LPS to "induce tolerance to toxic effects and to mobilize the host defenses in an immunologically nonspecific fashion." Its teachings involve principles of inflammation that can be applied to other inflammatory disorders, such as allergy, where tolerance is desired. In the same way Liu et al. teaches on page 382 and throughout the reference that the timing of allergen exposure is important for future tolerance to allergens and that early exposure decreases allergic sensitization. The reference teachings can be used to determine optimal timing of allergen exposure.

Tulic et al., teaches the prevention of allergy in 8-10-week old PVG rats (as opposed to both previous Examiner's and applicant's prior assertion that the animals were mice) administered LPS in aerosol form either: 1 day prior to; 1, 2, 4, 6, 8, 10 or 12 days after; or 18 hours after sensitization with OVA allergen. 8-10 week old PVG rats are considered to be young adult rats (In particular, Materials and Methods, page 604 - 605).

The claimed invention only differs from the prior art teachings by the administration of **irradiated LPS** to **neonatal animals**.

Matricardi et al., specifically teaches that the administration of LPS is beneficial to treat allergy and that a less toxic LPS derivative with immunostimulating properties is preferred for treatment purposes due the severe endotoxic effects of LPS (In particular, page 468, section entitled 'Proposed rationale for use against allergies').

Bertok et al., teaches making irradiated LPS and that it is a less toxic form of LPS with retained immunostimulatory properties. While the reference is silent to the type of immune response stimulated by the irradiated LPS, it would now be considered a Th1 immune response based on its cytokine profile (In particular, page 214, section II, second paragraph; and page 215, Table 1).

Liu et al., specifically teaches ample data demonstrating that human exposure to endotoxins (i.e. LPS) early in life (less than two years) has been demonstrated to decrease allergic sensitization; and that frequent benign exposures to endotoxin early in life are expected to prime the immune response toward prevention of atopy, allergic disease and asthma (In particular, page 382, second column, last paragraph before section entitled 'Factors Influencing Childhood Endotoxin Exposure').

Therefore, one of ordinary skill in the art at the time the invention was made would have been motivated to treat the young adult 8-10 week old rats of Tulic et al, with irradiated LPS molecules as taught by Bertok et al. because said irradiated LPS molecules are immunostimulatory, less toxic derivatives of LPS, as Matricardi et al. taught is preferred for the treatment of allergy. One of ordinary skill in the art would be especially motivated to treat young humans with the teachings of Matricardi et al, Tulic et al. and Bertok et al. since Liu et al., recognizes that early benign exposure to LPS can be effective in preventing allergy, as exemplified by decreased allergic disease

incidence of children raised on farms and confirmed by page 3 of the instant specification.

From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

10. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nora M. Rooney whose telephone number is (571) 272-9937. The examiner can normally be reached Monday through Friday from 8:30 am to 5:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

October 3, 2006

Nora M. Rooney, M.S., J.D.
Patent Examiner
Technology Center 1600

MAHER M. HADDAD
PATENT EXAMINER